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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/852,968	05/10/2001	Eugene Y. Chan	C0989/7016(HCL)	5672
7590 05/29/2008				
Helen C. Lockhart c/o Wolf, Greenfield & Sacks, P.C., Federal Reserve Plaza 600 Atlantic Avenue Boston, MA 02210-2211				
EXAMINER				
MUMMERT, STEPHANIE KANE				
ART UNIT		PAPER NUMBER		
1637				
MAIL DATE		DELIVERY MODE		
05/29/2008		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

09/852,968

**Applicant(s)**

CHAN, EUGENE Y.

**Examiner**

STEPHANIE K. MUMMERT

**Art Unit**

1637

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 27 February 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 2, 115-122, 124, 130-156 and 161-177 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 115-122, 124, 130-156 and 161-177 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Applicant's amendment filed on February 27, 2007 is acknowledged and has been entered. Claims 1, 115, 130, 137, 147, 162 have been amended. Claims 3-114, 123, 125-129, 157-160 have been canceled. Claims 170-177 have been added. Claims 1-2, 115-122, 124, 130-156, 161-177 are pending.

Claims 1-2, 115-122, 124, 130-156, 161-177 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

**This action is made FINAL.**

### **NEW GROUNDS OF REJECTION as necessitated by amendment**

*The previous rejection has been amended to address the amendments to the claims and the newly added claims.*

### ***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 2, 115-122, 124, 130-156, 161-177 are rejected under 35 U.S.C. 112, first paragraph, because the specification is not enabling for the labeling of individual units in a polymer for determining the identity of each individual unit sequentially via linear analysis through a nanochannel. The specification is also not enabled for the identification of individual units through detection of signals from less than all linked units in a polymer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

“Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.”

#### The nature of the invention

Claims 1-2 are directed to a method for identifying individual units of a polymer, comprising moving a polymer linearly past a detection point and determining the identity of individual units by detecting a non-ion conductance signal from less than all linked units in a polymer through exposure of linked adjacent signal generating units. Claims 115-122 and 124 are directed to a method for characterizing a test polymer, comprising linked units that are sequentially exposed to an interaction station. Claims 130-146 are directed to a method of

determining order of units of polymers labeled with a light emissive compound and polymer dependent impulses are measured as the units of the polymer linearly pass a station. Claims 147-156 and 161 are directed to a method for analyzing a set of polymers of linked units, orienting the polymers in an electric field and moving the sets of polymers through defined channels including nanochannels. Claims 162-164 are directed to a method of identifying a marker attached to a polymer by detecting signals generated by individual labeled unit specific markers as distinguished over exposure of linked adjacent units of a single polymer. Claims 170-177 are directed to methods as previously claimed and described above, modified so that unit specific markers are detected. The invention is in a class of invention which the CAFC has characterized as “the unpredictable arts such as chemistry and biology.” *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

#### The breadth of the claims

The claims encompass a method directed to the identification of the specific units of a polymer, comprising moving the polymer relative to a ‘station’, obtaining polymer-dependent impulses or signals and determining the identity of the units based on the signal generated. Furthermore, the claims encompass polypeptides and nucleic acids.

#### Quantity of Experimentation and Guidance in the Specification

The quantity of experimentation in this area is large.

Regarding the potential for labeling of each individual unit of a polymer such as a nucleic acid, either extrinsically or intrinsically, the specification states that labeling steps which require

“that all four bases in the DNA be tagged with different fluorophores” would be “extremely unfavorable” due to steric hindrance (p.2, paragraph 16 of PgPub). Regarding four-color labeling schemes, the specification states “A four nucleotide labeling scheme can be created where the A's, C's, G's, and T's of a target DNA is labeled with different labels. Such a molecule, upon traversing an interaction station, will generate a linear order of signals which correspond to the linear sequence of nucleotides on the target DNA” (paragraph 266 of PgPub). The specification also states that some of the nucleotides may be intrinsically labeled to reduce steric hindrance and states “It is also preferred that when extrinsic labels are used with the four nucleotide labeling scheme that the labels be small and neutral in charge to reduce steric hindrance” (paragraph 266 of PgPub). Clearly, there would be a high degree of experimentation necessary to effectively label (intrinsically or extrinsically), detect or identify each of the linked units of the polymer.

Furthermore, the specification does not clearly establish the practice of identifying the specific units through the detection of signal from less than all linked units in the polymer. While the specification states, “In addition to information about a specific unit the methods of the invention may be used to identify greater than one unit at a time in order to provide information about a polymer. In one aspect the method is carried out by providing a labeled polymer of linked units, detecting signals from labeled unit specific markers of less than all of the linked units, and storing a signature of the signals detected to analyze the polymer. In this aspect of the invention each unit of the labeled polymer may be labeled with a unit specific marker or less than all of the units may be labeled with a unit specific marker (paragraph 295)”, the specification does not make it clear that the “information about a polymer” includes the

identification of individual units of a polymer, or how the signatures are correlated from the polymer to the individual units. Therefore the specification also does not make it clear how to implement this embodiment of the method and it would require undue experimentation to achieve this embodiment of the method based only on the teaching of the specification.

Furthermore, the specification does not clearly define the practice of identifying the specific units through intrinsic label(s) that distinguish individual units of a polymer, without using ion conductance measurements. For example, the specification states "The polymer or at least one unit thereof is in a form which is capable of interacting with an agent or station to produce a signal characteristic of that interaction. The unit of a polymer which is capable of undergoing such an interaction is said to be labeled. If a unit of a polymer can undergo that interaction to produce a characteristic signal, then the polymer is said to be intrinsically labeled. It is not necessary that an extrinsic label be added to the polymer" (paragraph 157 of PgPub). The specification teaches broadly that "Many naturally occurring units of a polymer are light emitting compounds or quenchers. For instance, nucleotides of native nucleic acid molecules have distinct absorption spectra, e.g., A, G, T, C, and U have absorption maximums at 259 nm, 252 nm, 267 nm, 271 nm, and 258 nm respectively" (paragraph 158 of PgPub). While the specification provides an example of a means of 'intrinsic' labeling of nucleic acids, there is no corresponding intrinsic property of amino acids provided which would serve as an 'intrinsic' label for the practice of the invention. Therefore, for the practice of the invention for polymers that do not comprise nucleic acid, there would be a high degree of experimentation necessary to identify intrinsic labels for individual units of polypeptide.

Furthermore, while the specification provides multiple labeling schemes (four color, three color, two color) incorporating both intrinsic and extrinsic labels, the specification does not clearly provide specific embodiments wherein a specific 'agent' present at the interaction station of the method of the invention is set to interact with a specific type(s) of label, both intrinsic and extrinsic and provides a measurable result. A variety of options are provided for the interaction, including the specific types of labels that are present in a nucleic acid or protein polymer, and includes a variety of 'agent' formats including electromagnetic radiation, a quenching source and a fluorescence excitation source (paragraph 31) and a variety of label formats including intrinsic labels (inherent features of purine versus pyrimidine nucleotides, for example) and extrinsic labels including fluorophores or radioactivity (paragraph 56). However, with these disparate and broad teachings, there would be a high degree of experimentation necessary to establish the specific and detailed process of building the specific apparatus necessary for the practice of the invention and establishing the method of identifying and distinguishing individual units of intrinsically labeled and linked nucleotide units in a sequential manner - in addition to providing results for units that are labeled in a more conventional extrinsic manner.

Regarding the formation of the nanochannel pores and their application to the practice of determining the sequence of individual units of a polymer through linear analysis, Applicant has given no indication that such an apparatus or device, comprising nanochannels or a nanoplate has been reduced to practice. A post-filing reference, Chan (Chan, Eugene, Mutation Research, 2005, 573, p. 13-40) notes that "a single-base resolution strategy has yet to be articulated with solid-state nanopores" (p. 30 col. 2 to p. 31 col. 1). The Court in *In re Ghiron*, 442 F.2d 985, 991, 169 USPQ 723, 727 (CCPA 1971), made clear that if the practice of a method requires a